Title	Follow-Up Studies of Long-Term Survivors in Biliary Atresia
Author(s)	CHIBA, TSUNEO
Citation	日本外科宝函 (1987), 56(3): 289-295
Issue Date	1987-05-01
URL	http://hdl.handle.net/2433/204030
Right	
Type	Departmental Bulletin Paper
Textversion	publisher

Arch Jpn Chir 56(3), 289～295, Mai, 1987

Follow-Up Studies of Long-Term Survivors in Biliary Atresia

Tsuneo Chiba

Division of Pediatric Surgery, Tohoku University Hospital, Sendai

Received for Publication, Jan. 12, 1987

Summary

Of the 234 patients with biliary atresia who received surgery at the Tohoku University Hospital, 38 were long-term survivors aged 10 years or more. Recently, we carried out a questionnaire survey on these subjects concerning their school and social life; they were also subjected to medical examinations. The following results were obtained: 1) The school life of patients was almost the same as that of healthy children, although some patients were obliged to lead a restricted school life during elementary and junior high school. In terms of intelligence or mental aspects, no difference was noted between patients and healthy children. 2) In terms of height, the patients showed good growth, while some patients showed delayed increase in body weight. 3) In terms of secondary sex characters, no problem was found among cases. 4) Hepatomegaly and/or splenomegaly was found in a relatively large number of the cases. Patients with marked splenomegaly required some treatment. 5) Abnormalities in liver function parameters were found in a relatively large number of patients, indicating the necessity for long-term follow-up of biliary atresia patients even after patients have reached adulthood.

Introduction

It was in 1953 that the first surgical treatment of biliary atresia was carried out at the Tohoku University Hospital. This patient died of respiratory insufficiency postoperatively. The second patient survived the surgery; this patient, now 31 years old, is the oldest of all patients who received hepatic portoenterostomy in the world. In this paper, the results of a questionnaire survey which was carried out to investigate school or social life of the patients who survived more than 10 years after surgery and results of the analysis of their recent laboratory examinations are reported.

Subjects and Methods

Up to October 1986, 234 patients with biliary atresia have been surgically treated at the Tohoku University Hospital. As of October 1986, 98 patients are alive, of whom 38 are 10 years

Key words: Biliary atresia, Long-term survivors of biliary atresia, Prognosis of biliary atresia.
索引語：先天性胆道閉鎖症，胆道閉鎖症長期生存例，胆道閉鎖症の予後
Present address: Division of Pediatric Surgery, Tohoku University Hospital, 1-1 Seiryocho, Sendai 980, Japan.

old or more (24 between 10 and 15 years, 7 between 16 and 20 years, 5 between 21 and 30 years and 2 over 30 years). The main type of extrahepatic bile duct was Type I in 11 cases (including 9 Type Icyst cases), Type II in 3 cases and Type III in 24 cases. Of these patients, 7 received hepaticojejunostomy, 27 received hepatic portojejunostomy and 3 received hepatic portocholecystostomy.

Of the 38 patients, 31 are now students and the remaining 7 have an occupation. A questionnaire was sent to these patients to inquire about their school or social life. In inquiring about school life, the subjects were asked to answer not only about their life in the schools from which they had already graduated. For example, senior high school students were invited to answer also about their life in elementary and junior high schools. Answers to the questionnaire were collected from 30 of the 33 patients whom we asked to give answers (the remaining 5 patients were excluded from the study because they became 10 years old during the survey). Furthermore, medical examinations were carried out on these patients. On the basis of these data, we analyzed the long-term survivors. We also evaluated two patients who died at age over 10 years (one of them died of rupture of esophageal varices at the age of 16, and the other died of hepatic failure at the age of 28).

Results

Table 1 shows the relationship between the age at the operation and long survival. Of the 149 patients who received a radical operation during the same period, 38 (25.5%) were alive. For the patients who received surgery at age below 60 days, the survival rate was 75%, while the rate was below 35% for patients receiving surgery at age over 60 days. Thus, the survival rate decreased with an increase in age at surgery. *Growth*: Both in males and females, the height was almost the same as or greater than the nationwide average (Fig. 1). Thus, growth was generally good. A 31-years-old woman showed poor growth because of repeated ileus and the development of eventration of the diaphragm and malabsorption was noted among individuals (Fig. 2). Extremely low body weight patients were found in females. It is noteworthy that many of these low-weight cases belonged to correctable type. A possible cause of low body weight in these cases is postoperative complications.

Menstruation was noted in all females including the one with Turner's syndrome. Menarche occurred at the age of 12 years in 5 cases, 13 years in 1 case, 15 years in 1 case, 16 years in 2 cases and 17 years in 1 case. The menstrual cycle was regular in 7 cases and irregular in 3 cases. Growth of the breast and public hair was almost normal in all females except for the one with

Table 1. Age at operation and long-term survivors.

Age at op.	Cases	Survivors
—60 days	20	15(75%)
61—70	23	8(34%)
71—90	39	8(23%)
91—	67	7(10%)

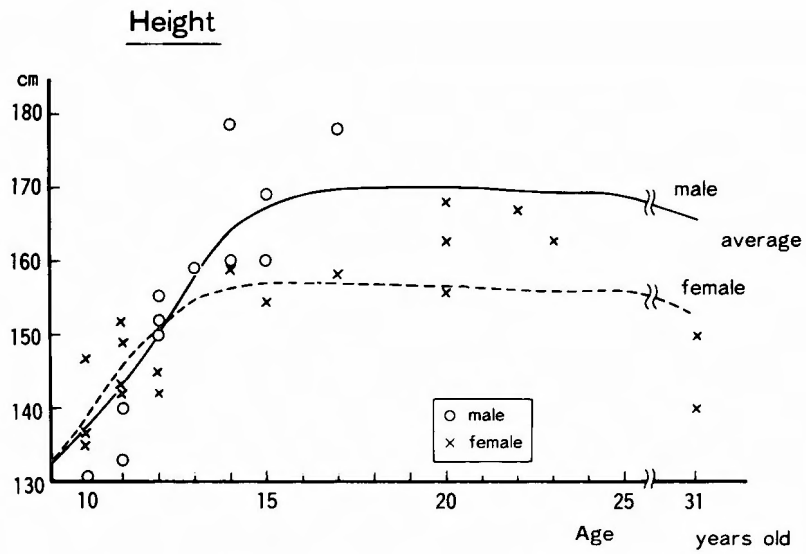

Fig. 1. Height of the long-term survivors in biliary atresia.

TURNER's syndrome. Secondary sex characters seemed to be normal also in males. However, males need to be further followed up because the oldest surviving patient in the present study was only 16 years old. One man, who died at the age of 28 years, got married and had a son before death.

School life and social life: Excluding one case of mental disorder, all patients of school age were attending ordinary schools. In elementary and junior high schools, some patients were occasionally absent from school or attended the school only for half a day (Table 2). In senior high school or schools of higher grade, patients had no difficulty in attending the school. Most

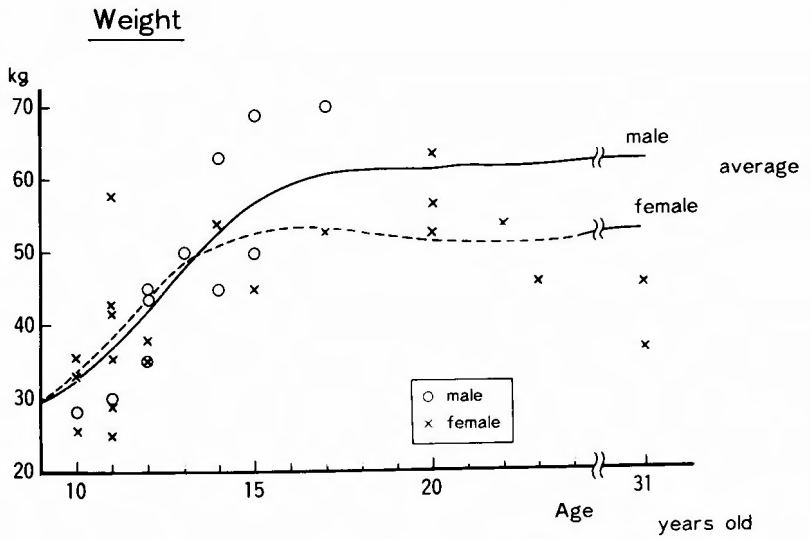

Fig. 2. Weight of the long-term survivors in biliary atresia.

Table 2. School life of long-term survivors in biliary atresia.

	Elementary school	Junior high school	High school	College or university
Attendance				
All school days	24	12	9	2
Almost all days	4	3	0	0
Half a day	1	0	0	0
Physical training				
Received	23	11	6	2
Except hard training	3	0	1	0
Not received	3	4	2	0
School record				
Grade A	9	3	2	2
Grade B	17	9	6	0
Grade C	3	3	1	0
Extracurricular activities				
Sports club	11	9	2	0
Others	14	4	4	2

of the patients received ordinary physical training at school, although some received no physical training. School records were equal to or better than the average, presenting no difference from those of healthy students. Analysis of the data concerning extracurricular activities disclosed that patients belonged to sports clubs at school (including very active sports clubs). However, patients with jaundice or pancreatitis did not seem to be enjoying school life. Seven adults had an occupation (public official, computer programmer, bus conductress, etc.). All of them were attending their place of job regularly.

Medical examination: Hepatomegaly was found in 6 (16%) of the 38 patients, but it was mild in all but one case (Table 3). All patients with hepatomegaly were less than 12 years old. Three of these 6 patients had prolonged jaundice. Splenomegaly was found in 19 patients. Of these 9 patients, the oldest was 15 years old, and most of them were less than 12 years old. Other 5 patients had received splenectomy with vascular surgery because of portal hypertension. Hepatosplenomegaly was noted also in the two patients who died at the age of over 15 years, respectively.

By liver function tests, 4 patients were found to have serum bilirubin levels of 2 mg/dl or more. One of these 4 had prolonged jaundice which had started in infancy; in the remaining

Table 3. Hepatosplenomegaly in long-term survivors of biliary atresia.

Age (years old)	Patients examined	Hepatomegaly	Splenomegaly
20 or more	7	0	0(1)
15—19	7	0	1
10—15	24	6	7(4)

( ): Splenectomized patients

Table 4. Number of patients who showed abnormal laboratory examinations.

Age	Cases	Bilirubin	GOT	GPT	AL-P	γ-GTP	ZTT	TTT
20 yrs-	5	1	0	0	1	1(1)	3(1)	0
15—19	5	2(1)	1	1	3(1)	1	3(1)	0
12—14	9	3(1)	6(3)	6(3)	8(4)	6(3)	4(2)	2(1)
10—11	11	3(3)	6(6)	7(7)	11(9)	6(6)	7(6)	5(5)

( ): Patients who had a history of ascending cholangitis

3 cases, jaundice disappeared once, but it recurred thereafter. Serum bilirubin levels between 1.1 and 1.9 mg/dl were found in 5 patients. The remaining 29 patients had serum bilirubin levels of 1 mg/dl or less. All of the patients showing bilirubin levels of 2 mg/dl or over had a history of ascending cholangitis.

Abnormal GOT was noted in 13 of the 30 patients examined, while abnormal GPT was found in 14 patients (Table 4). Twelve patients (38%) were found to have both abnormal GOT and abnormal GPT. Abnormal GOT or GPT values were found frequently in patients aged below 14 years. The same tendency was seen in the levels of γ-GTP and TTT. On the other hand, many patients showed abnormally high levels of alkaline phosphatase and ZTT. Ascending cholangitis is considered to have deep relationship to the abnormal data.

Fig. 3 shows the relationship between the levels of GOT and the age at operation in long-term survivors. Almost all of the patients who showed abnormal high levels of GOT have portal hypertension. This tendency was seen in the levels of alkaline phosphatase, ZTT and γ-globulin. Ascending cholangitis and portal hypertension have severe effects on their liver function for a long time. However, abnormal levels of these examinations usually fall to normal range with the age and all patients whose age were 15 or more showed normal levels of these examinations.

Esophageal varices were found in 11 (41%) of the 27 patients examined. Of these 11

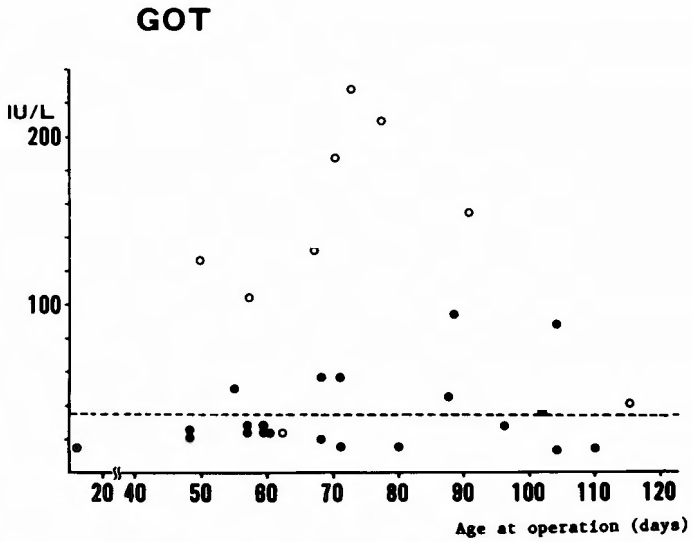

Fig. 3. Levels of GOT and age at operation in long-term survivors.

patients, 9 had a history of ascending cholangitis. Varices were found in all of the 4 patients having jaundice. Three patients had a history of bleeding from esophageal varices. An additional two patients, who died at age over 10 years, had a history of bleeding from esophageal varices.

Comment

In recent years, reports on long survival of biliary atresia patients have been increasing[1,2,3]. Since the oldest survivor of this disease is still 31 years old, it is necessary to make a general evaluation of the results obtained from multiple follow-up studies.

In the present study, the height of patients aged 10 years or over was equal to or above the average, while relatively many patients showed a body weight below the average. The high incidence of low body weight seems to be related to complications, but it is not clear why low body weight was often seen in patients with correctable type. This may be explained by the fact that survival from this disease was possible mainly in patients with correctable type in the past, and that both height and weight of the patients reach the averages at the age of 4–5 years. However, delayed nutritional recovery, observed in some cases, also seems to be related to such a high incidence of low body weight.

During elementary and junior high school, some patients were obliged to lead a restricted school life, but most of the patients could lead a normal school life. Many patients were able to receive ordinary physical training and take part in extracurricular activities like healthy children. However, patients with prolonged jaundice or those with complications did not always enjoy school life. No problem was seen regarding inteligence or mental aspects[2]; hence, it was possible for patients to enter senior high school and university and to get jobs requiring intelligence.

Hepatomegaly and/or splenomegaly was found in a relatively large number of cases[2,3]. The incidence of splenomegaly was as high as 14/38 (37%) and it was found to be closely related to ascending cholangitis and portal hypertension[4]. Splenomegaly in older patients was different from that seen in the early postoperative period. In older patients, splenomegaly showed hardly any tendency or reduction even in the absence of jaundice. Many of the older patients with marked splenomegaly required some treatment such as splenectomy and partial splenic embolization. This is an issue for older patients.

Esophageal varices were found in 41%. Along with splenomegaly, the presence of esophageal varices is an important sign of portal hypertension; hence, it should be always checked in observation of the patient's progress. Esophageal verices are closely related to ascending cholangitis[5]. However, since there are many patients who have no history of ascending cholangitis but develop esophageal varices, periodical esophagoscopy is necessary for several years after surgery. However, at ages over 5 years, the development of varices is quite rate in patients having no ascending cholangitis or portal hypertension. Therefore, esophageal varices need to be checked chiefly in ascending cholangitis- or portal hypertension-positive cases.

It is generally known that parameters of liver function become normal with increase in

age[2,3,6]. However, in our latest follow-up studies, older patients did not necessarily show changes in some parameters; instead, patients who once showed abnormal values tended to retain such abnormalities. Abnormalities in transaminase, alkaline phosphatase, ZTT, TTT, γ-GTP and LAP were found in a relatively many number of patients. This finding indicates the necessity for long-term follow-up of patients[7]. Abnormalities in these parameters were found not only in patients with ascending cholangitis but in patients with portal hypertension.

Eventful course after surgery is another cause of these abnormalities. Therefore, physicians in charge of biliary atresia patients have the responsibility to observe these patients carefully to determine what pathological roles these abnormalities will play in the future.

References

1) Howard BR, Driver M, McClemend J, et al: Prolonged survival after operation for extrahepatic biliary atresia. In Biliary Atresia and Its Related Disorders, edited by Kasai, M., Excerpta Medica, Amsterdam-Oxford-Princeton, pp 167–173, 1983.
2) Kasai M, Hanamatsu M, Ohi R, et al: The follow-up studies of 26 cases with biliary atresia surviving more than 10 years after successful operation. J Jap Societ Pediatr Surg **21**: 1133–1144, 1985.
3) Akiyama H, Saeki M, Ogata T: Long term survivors in biliary atresia: An analysis of 21 cases living more than 10 years. J Jap Societ Pediatr Surg **22**: 586–596, 1986.
4) Arai T, Suruga K, Fukuda Y: Significant role of the ascending cholangitis in the etiology of the portal hypertension after the radical operation for congenital biliary atresia. Jap J Pediatr Surg **12**: 1051–1058, 1980.
5) Akiyama H, Saeki M, Ogata T: Portal hypertension after successful surgery for biliary atresia. In biliary Atresia and Its Related Disorders, pp 276–282, 1983.
6) Chiba T, Hanamatsu M, Mochizuki I, et al: Follow-up studies on the long-term survivors of biliary atresia: Clinical aspects. In Biliary Atresia and Its Related Disorders, pp 239–248, 1983.
7) Chiba T, Mochizuki I, Sawa N, et al: Important role of long-term follow-up after surgery for biliary atresia. Jap J Pediatr Surg **16**: 841–846, 1984.

和文抄録

先天性胆道閉鎖症の長期生存例に関する研究

東北大学医学部小児外科

千　葉　庸　夫

東北大学において1953年以降経験した胆道閉鎖症手術例は234例で，そのうち38例が10年以上の長期生存例である。最年長例は31才で，現在７人が職業を有し，その他は学校生活を送っている．これら38例に，10才以降に死亡した２例を加え長期生存例の検討をおこなった．その結果，

1) 学校生活では殆どの例で健康な子供と変わらない生活を送っており，成績も良好であるが，黄疸例や，術後の合併症のある例では，学校生活にも制限がみられる．

2) 身長や体重も多くの例では平均かそれ以上であるが，女児では低体重例がめだつ．

3) 肝，脾腫が残っている例が多く，食道静脈瘤も４割の例にみられる．

4) 肝機能検査では，年齢とともに正常となる例もみられるが，15才を過ぎても異常値を示す例がかなり多く，注意して観察すべきである．